

## Non-Technical Abstract

Protocol Title: *Clinical Protocol for Modification of Tumor Suppressor Gene Expression and Induction of Apoptosis in Non-Small Cell Lung Cancer (NSCLC) with an Adenovirus Vector Expressing Wildtype p53 and Cisplatin*

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The purpose of this protocol is to study a way of stopping cancer causing genes from functioning in human lung cancer cells in patients. One gene that is commonly altered in human lung cancer is the p53 tumor suppressor gene. A mutation or deletion of both copies of this gene causes the cell to become cancerous.

This protocol uses a gene therapy technique to replace the normal function of the p53 gene. The normal p53 gene will be introduced into lung cancer cells. This normal gene will overcome the function of the mutant gene and also replace the normal p53 function.

A novel feature of this protocol is that the gene will be introduced into human cancer cells in the patient by an adenovirus. A special adenovirus that is harmless to patients and rendered incapable of dividing is used. The adenovirus is taken up by the cancer cell but is not integrated into the cancer cell's DNA. The newly inserted gene is now expressed for a short period of time. This burst of expression by the p53 gene renders the cancer cell incapable of growing and dividing and the cell initiates a program that leads to its death. A common chemotherapy agent (drug) called cisplatin will be given along with the adenovirus. The adenovirus potentiates the cancer killing ability of this drug. The normal p53 gene is not harmful to normal cells. The adenovirus will be injected directly into the lung cancer.

Patients with lung cancer who are unable to have surgery, radiation therapy, or chemotherapy may participate. The tumor will be tested to determine if it has one or the other genetic abnormality. The adenovirus capable of correcting the specific gene abnormality will be directly injected into the tumor. One injection will be of the adenovirus alone and the second injection will be of the adenovirus followed by intravenous administration of the cisplatin. Following this the growth of the tumor will be measured. The tumor will also be studied to determine if the tumor cells are taking up the adenovirus.